IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Dharmaraj Ramachandra RAO

Serial No.: 10/539,415

Filed: March 20, 2006

Confirmation: 2363

Group Art Unit: 1626

Examiner: Yong Liang CHU

For: **PROCESS FOR PREPARING DULOXETINE AND INTERMEDIATES FOR USE THEREIN**

REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

Applicants request reconsideration of the rejections set forth in the Office Action mailed February 29, 2008. Filed of even date herewith is an extension of time together with the appropriate government fee, therefor, in order to make this request for reconsideration timely.

Claims 1-6 are pending and claims 18-23 are withdrawn from consideration as being directed to non-elected inventions.

Claims 1 and 2 stand rejected under 35 U.S.C. §102(b) allegedly as being anticipated by Robertson et al (U.S. Patent No. 4,956,388). Robertson et al disclose:

- duloxetine and salts thereof;
- (±)duloxetine and salts thereof ;
- racemic duloxetine oxalate (±)duloxetine oxalate and (-)-duloxetine oxalate;
- (±)duloxetine maleate

However, there is no disclosure of how the separate isomers of duloxetine are resolved, how the separate isomers of the salts of duloxetine, generally, are prepared, nor of how separate isomers of duloxetine oxalate and duloxetine maleate, specifically, are prepared. Although, the Examiner cites to Example 14 in Column 11 as disclosing a

process for preparing (+)duloxetine, that disclosure only names the compound and does not disclose the process for its preparation. Column 5, lines 46-55 are to general resolution techniques, but do not teach the chiral acids specified in claims 1-2. Thus, there is no specific disclosure of any process for preparing (±)duloxetine, or an acid addition salt thereof, which process comprises resolving racemic (±)duloxetine with a chiral acid to obtain a salt of the chiral acid and (+)duloxetine, substantially free of (-)duloxetine. Claims 1 and 2 are, therefore, novel over the Robertson et al disclosure.

It is elementary patent law that in order to be anticipatory the disclosure of a reference must be enabled i.e., must teach one how to make and use the claimed compounds; see generally Chisum on Patents, 1:304[1][c] and See *In re Brown* 329 F.2d 1006, 1010-11, 141 USPQ 245 (CCPA 1964). Withdrawal of the rejection is therefor respectfully requested.

Reconsideration of the previous rejections of claims 1-6 under 35 U.S.C. §103(a) as unpatentable over Robertson et al in view of the teachings of U.S. Patent No. 3,830,806, and Wheeler et al *Journal of Labelled Compounds and Radiopharmaceuticals,* 1996, Vol. 36, 3, pp.213-223, (hereinafter Wheeler et al) is respectfully requested.

Again, although the Examiner refers to Robertson et al example 14 (column 11) and column 5, lines 46-55, example 14 does not teach a process for producing the main compound, but only names the compound itself. Column 5, lines 46-55 identify racemic mixtures of optically active isomers generally, but do not identify the resolution of the (+)duloxetine and clearly not a resolution of the (+)duloxetine, substantially free of (-)duloxetine. There is no description of the chiral acids of claim 2 or indeed of any chiral acids at all. Thus, Robertson et al is a nonenabling disclosure for the claimed process of claims 1-6.

The secondary references do not correct the foregoing deficiencies.

For example, the '806 patent does not relate to duloxetine or its derivatives and merely discloses optically active acids including dibenzoyl tartaric acids that can be used for resolving racemic mixtures. It does not teach the useful resolution of compounds such as (+)duloxetine and not for (+)duloxetine substantially free of (-)duloxetine. There is no teaching of how this resolution would be carried out.

Similarly, the Wheeler et al publication, which discloses C14 isotopes of duloxetine hydrochloride and its preparation by an asymmetric synthesis involving chiral reduction using borane, does not disclose the process of the invention. Although, Wheeler teaches the clinical application of a duloxetine hydrochloride salt, there is no disclosure of any means for resolving and recovering (+)duloxetine isomer, especially one "substantially free" of (-)duloxetine acids as claimed.

The Examiner is only utilizing hindsight reconstruction with the benefit of Applicants disclosure as a guide to pick and choose isolated teachings from the prior art in order to attempt to provide enablement to the Robertson et al patent. However, since none of these isolated teachings provide enablement for the Robertson et al disclosure, the process of obtaining the claimed isomers, substantially free of unwanted isomer, does not correct the foregoing deficiency inherent in the nonenablement of a process of obtaining the isomers of interest. For the foregoing reasons, under 35 U.S.C. §103(a) the obviousness rejection also must fail for lack of enablement and withdrawal of all rejections of claims 1-6 and passage of this application to issue is respectfully requested.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith, or credit any overpayment, to our Deposit Account No. 14-1437, under Order No. 8693.009.US0000.

Respectfully submitted,

TPP/tnj
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